OSTEOGENESIS IMPERFECTA AND IDIOPATHIC FRAGILITAS OSSIUM.

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ABNORMAL idiopathic fragility of the bones as a definite disease has been recognized for many years, and the condition has been described more or less perfectly by many observers. The disease may be divided into two main groups (1) symptomatic fragilitas ossium, in which the abnormal fragility of the bones is due to some local or well recognized general condition, and (2) the idiopathic form, often termed osteopsathyrosis.

Symptomatic fragilitas ossium due to local conditions is seen following bone tumors, such as sarcoma, metastative cancer, bone cysts, and, most markedly, in multiple myeloma, or sometimes as the result of inflammatory processes, as osteomyelitis or gumma. It is seen also in certain general systemic bone diseases, as rachitis, and osteomalacia. It is said to occur in congenital syphilis, but there is some doubt whether syphilis, except in the form of a gumma, ever affects the bones sufficiently to cause fracture. In certain nervous and mental diseases, abnormal fragility of the bones is known to occur, fractures being caused by the slightest violence. This is marked in insanity and tabes, and in these cases, as pointed out by Charcot, it is probably due to a trophic disturbance. Pathological fractures have been reported occurring in cases of scurvy, and they are not uncommon in the aged, where they are due to the osteoporosis of old age. The above mentioned causes of abnormal fragility are well recognized, and the condition itself is of relatively minor importance.

Comparatively little, on the other hand, is known of idiopathic fragilitas ossium, and the etiology of many of the cases is still obscure. It was first differentiated from osteomalacia and the symptomatic forms by Lobstein[2] in 1883, who suggested the term osteopsathyrosis for the condition, and it has generally been known by this name since, or as periosteal dysplasia (Schuchardt[3]). It may be defined as a condition of macroscopic and microscopic osteoporosis of unknown cause, producing a fragility of the osseous system, resulting in multiple fractures. Gurlt[4] in 1862 wrote a classical article on the subject, and since then many articles have appeared, among which may be mentioned those of Schultz,[5] Linke,[6] Griffiths,[7] Schuchardt, Biggs,[8] Trendelenberg,[9] Nathan,[10] and Broca and Herbinet.[11] Griffiths collected from the literature 57 cases, several of which, however, are probably not true idiopathic fragilitas ossium.

The following two cases were treated in the wards of the Massachusetts General Hospital, and are reported through the courtesy of the physicians in whose services they occurred.

Case I.—Service of Dr. A. T. Cabot. Female, 13, single. Massachusetts General Hospital. No. 145,787. December 30, 1905.

Family History.—Mother and father well. None of her relations have been subject to fractures. One brother, 11 years old, perfectly well. No evidence of syphilis in the family.

Previous History.—Chicken pox and whooping cough, but otherwise always well. She has had fractures as follows:

(1) At birth, right humerus; (2) at five years, right femur just above condyles; (3, 4) between five and eight years, broke left lower leg at about centre twice during these three years, but does not remember exact dates; (5) at eight years, broke left tibia again at about same place; (6) at twelve years, hit elbow and "sprained it;" no pain in particular, and no treatment; X-ray shows a fracture of the olecranon; (7) three months ago, broke left tibia at about same place for fourth time; (8) December, 1905, broke right femur above condyles; (9) February, 1906, broke left femur above condyles.

Of the earlier fractures she does not remember a great deal. Fracture No. 5, the third fracture of the left lower leg, was caused by a fall, but the mother says it appeared as if the fall were in consequence of the leg breaking, instead of the fracture being caused by the trauma. Fracture No. 7 occurred three months before her admission to the hospital, and happened in the same manner. When not recovering from fractures the child has attended school, played with other children, and has been in every way normal. She has been in bed since September, 1905, recovering from fracture No. 7, and previously to that she had worn a leather brace on her left leg. The fractures as well as she can remember, have been accompanied with the classical symptoms to a greater or less extent, but pain and swelling have never been marked. The lack of pain is well illustrated in fracture No. 6, the olecranon, which caused so little inconvenience she did not seek treatment.

At birth she was a healthy baby, and nothing abnormal was noticed, the fracture of the humerus, occurring at delivery, being looked upon as an obstetrical accident. Her appetite has been normal, and her diet that of well to do country people, and the same as the rest of the family.

Present Illness.—Last night was awakened by a sharp pain in her right thigh, which on examination proved to be due to a fracture of the femur.

Physical Examination.—Head large and square. Posterior fontanelle depressed, two inches in diameter and soft, but no pulsation felt. Anterior fontanelle closed. Poorly developed and pale. Pupils equal, and react to light. Throat and mouth normal. Heart and lungs and abdomen not remarkable. No rachitic rosary. Right arm shows slight bowing at lower third of the humerus. The elbow shows an old fracture of the olecranon with considerable separation of the fragments, but no limitation of motion or other functional disability. Left arm normal. Right lower leg shows anterior bowing at the junction of the lower and middle third, with some motion (fracture No. 7). Right femur shows a fracture at the junction of the middle and lower third with crepitus, abnormal mobility, etc. The radiograph shows an irregular fracture, not transverse, with little displacement. Epiphyses throughout the body normal.

Fracture put up under ether in Buck's extension, with Desault, and coaptation splints. On February 14, 1906, the Buck's extension was removed and, union being firm, the leg was put up in a plaster spica.

On February 15, at 5 A.M., the patient woke up with a sharp pain in her left leg, and on examination a fracture was found just above the condyles of the left femur. The fracture was treated as the other had been. On March 16 the spica was removed from the right leg, and union found solid.

On April 1 there was fair union in the left femur, and the leg was put up in a plaster spica.

Urine.—December 31, 1905. Pale, cloudy, acid. Specific gravity 1033. No sugar or albumin.

April 3, 1906. Amount in 24 hours 1350 cc. Color pale. Reaction acid. Specific gravity 1007. Urea, 1.13 per cent., 15.25 grams; uric acid, .033 per cent., .45 grams; chlorine, .267 per cent., 3.60 grams; phosphoric acid, .081 per cent., 1.29 grams; sulphates, .012 per cent.; sugar, 0; albumin, very slight trace; sediment, not remarkable.

This specimen shows a dilute urine, although the patient had been on extra diet and tonic treatment for nearly two months. The sulphates particularly are considerably diminished, the normal being about 2 per cent. The proportion of uric acid to urea is high.

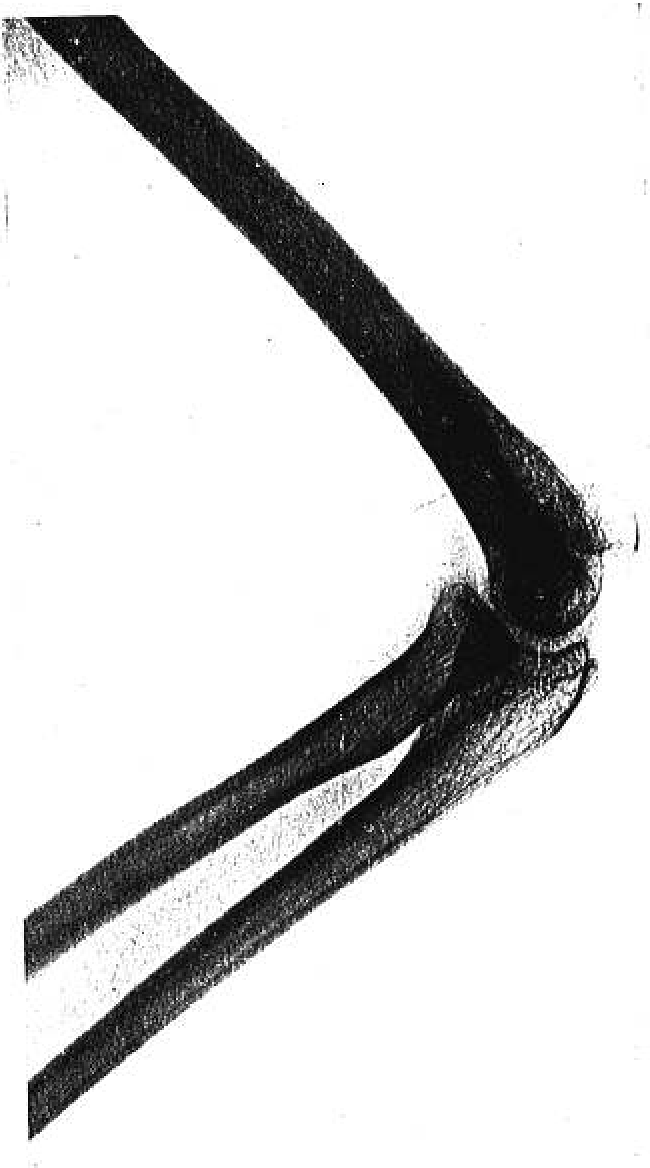
April 18. Amount in 24 hours 720 cc. Color normal. Reaction acid. Specific gravity 1020. Urea, 3.15 per cent., 22.6 grams; uric acid, .07 per cent., .5 grams; chlorine, .503 per cent., 3.6 grams; phosphoric acid, .15 per cent.,; sulphates, .125 per cent.; sugar, 0; albumin, very slight trace; sediment, not remarkable. This specimen is practically normal.

A description of the radiographs taken during the month of March is as follows:

Head.—A lateral view only was taken, which shows its peculiar shape, but nothing abnormal about the bones could be detected.

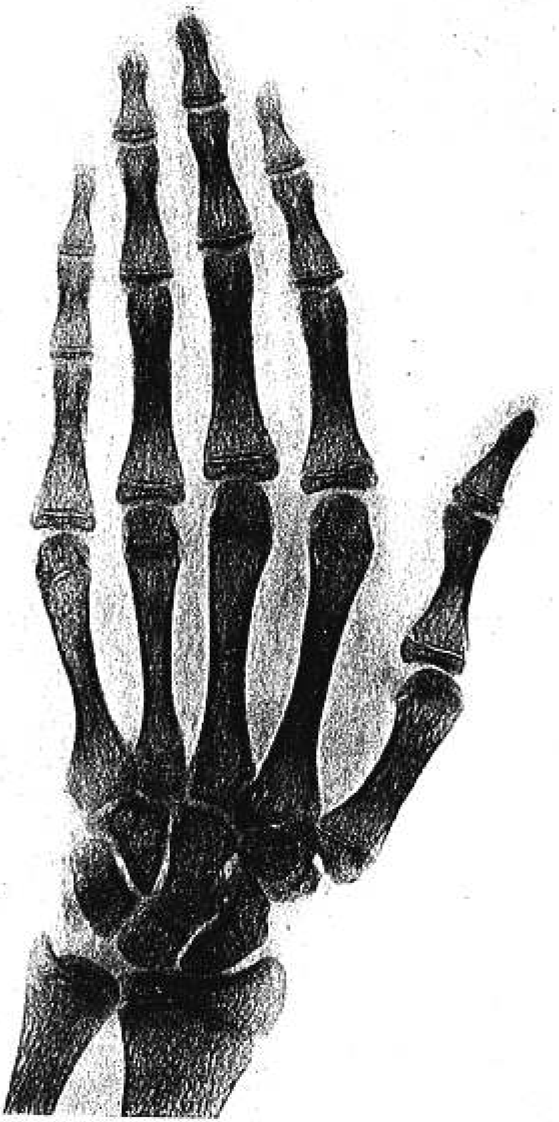
Upper Extremities.—An X-ray of the right shoulder showed the ribs, clavicle, and scapula normal. The humerus also appeared normal, except near the head, where there was some thinning of the cortex, and evident diminution in the lime salts in the central portion of the bone. The shaft cast a dense shadow, and the relation of the cortex to the medulla was normal. The radius and ulna (Fig. 1) were also normal, except that the upper extremity of the latter bone had somewhat the same appearance as the head of the humerus, although in a less degree, and there was

FIG. 1.



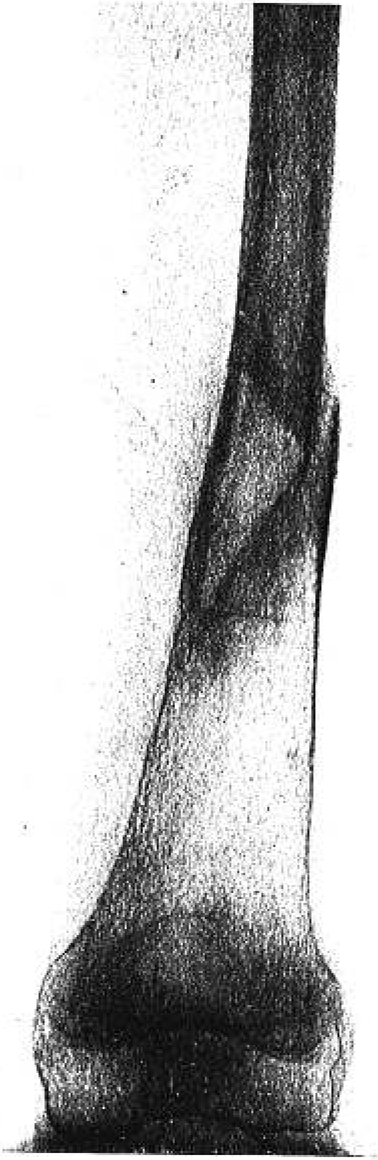
Case I.—Right arm. The shafts of the bones are normal, but the head of the ulna casts a somewhat fainter shadow than is usual. Ununited fracture of the olecranon.

FIG. 2.



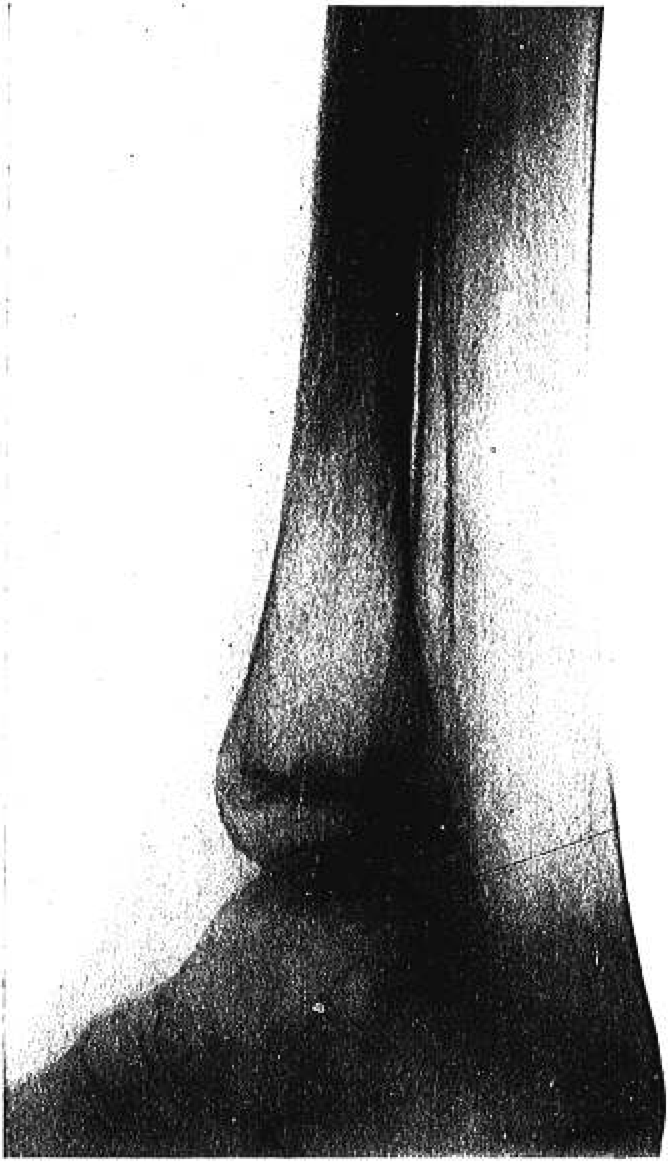
Case. I.—Hand.

FIG. 1.



Case I.—Left femur. Marked thinning of the bone below the fracture.

FIG. 4.



Case I.—Right ankle.

an ununited fracture of the olecranon. The bones of the hand cast a somewhat fainter shadow than would naturally be expected, and the first phalanges were extremely long (Fig. 2).

Lower Extremities.—X-rays of the thighs showed the upper parts of the bones normal. On the right there was an oblique fracture 4 inches, and on the left a transverse fracture 3 inches (Fig. 3) above the epiphysis. The epiphyses about the knee were normal. From above the points of fracture to the ends, the bones cast a comparatively faint shadow, the appearances not being due to a high tube, but apparently to a lack of bone substance. The cortex was thin in the lower third of the bones, and the medulla proportionately larger. The widening of the medullary cavity was more marked, and abrupt on the right than on the left (Fig. 4). The fibulæ were small.

The tibiæ had at their upper and lower extremities a similar appearance to the upper end of the humerus, and lower end of the femori, and the appearance might be said to be somewhat similar to the changes seen after long immobilization of a limb in cases of prolonged tubercular bone disease. Some deformity from the old fractures could be seen in the shafts. Nothing comparable to a localized bone disease could be seen in any of the bones.

The patient received while in the hospital general tonic treatment. She was put on " extra diet," and was given cod liver oil and eisenzucker. During January she received small doses of thyroid extract three times a day, but this was later discontinued, and a syrup of manganese substituted.

Case II.—Service of Dr. H. A. Towle. Female, ten months. Entered the skin ward of the Massachusetts General Hospital May 31, 1905.

Family History.—Father and mother well. One sister, four years old, and a brother two and a half years old, perfectly well.

Previous History.—At birth nothing abnormal was noticed, and for the first nine months the child was healthy and took nourishment well. One month before admission began to lose weight, and developed a skin eruption. The parents, Syrians, never noticed anything unusual about the bones.

On admission to the hospital the diagnosis of dermatitis was made, and the child treated accordingly with good effect; but about July 1 she developed a chronic bronchitis from which she died July 15.

Abstract of Autopsy.—July 16, 1905. Dr. Oscar Richardson. Anatomical diagnosis: Purulent bronchitis, anæmia, œdema of piæ, multiple fractures, osteoporosis. The body was that of a female child, much emaciated, 62.5 cm. long.

Head.—Anterior fontanelle open, posterior nearly closed. Pia moderately infiltrated with thin clear fluid. Vessels normal. Nothing remarkable about the brain or cord.

Trunk and Extremities.—The epiphyses of the long bones were slightly enlarged. The shafts of the long bones of the extremities showed deformity and multiple fractures. On section the bones cut easily with the knife, and the distribution of the cortical bone was uneven, it being in many places entirely absent. In no bone was it of normal thickness. The medullary cavities were large and filled with soft red marrow. There was little subcutaneous fat, and the muscles were pale.

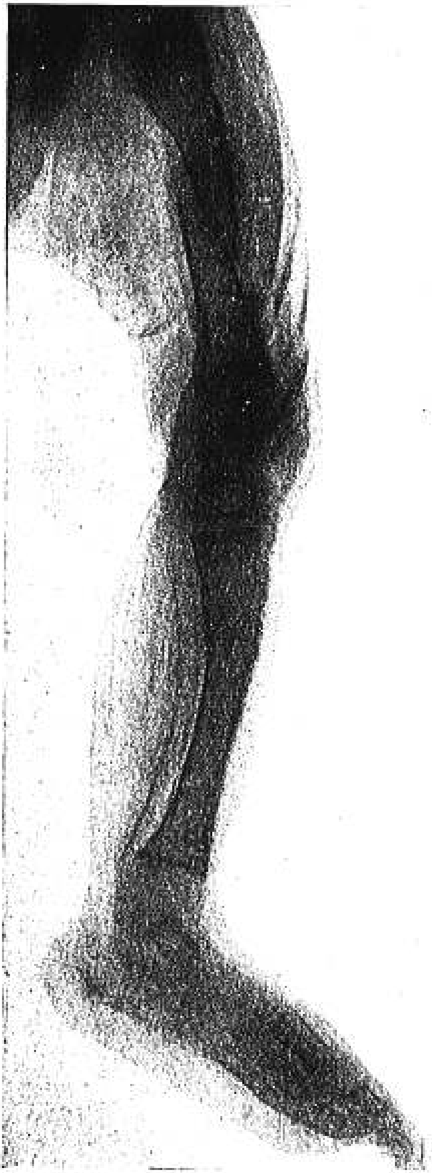
Digestive tract and abdominal organs normal. Pleura smooth. Heart normal. The mucous membrane of the trachea and bronchi was red, thickened and bathed in considerable yellow purulent material. No areas of consolidation were found in the lungs.

Microscopic examination of sections from several of the bones showed practically the same condition. The cortical bone was thin, and the medullary cavity proportionately large, while the periosteum was thick and fibrous. The Haversian canals were large. There seemed, however, to be a normal number of osteoblasts, and but few osteoclasts were seen in an examination of several sections. The marrow was not remarkable, and contained fat, myelocytes and giant cells in normal proportions. In other words, nothing abnormal was noted except a lack of bone. A section through an epiphysis showed the cartilage forming bone in the usual manner.

Radiographs were taken post mortem, and showed from one to four fractures of each of the long bones of the extremities (Fig. 5) with some displacement. These fractures were nearly all transverse. The clavicles were normal, as were also the ribs.

The bones all showed the same condition. The cortex was extremely thin, and in places seemed to be absent, and the bones cast a faint shadow, which was evidently due to a lack of lime salts. The general appearance of the bones was similar to that in Case I.

FIG. 5.



Case II.—Radiograph, lower extremity. The multiple fractures and extreme thinning of the bone are clearly seen.

Lobstein, who first separated the idiopathic variety from other forms of fragilitas ossium, described it as a concentric atrophy of the bones with enlargement of the marrow cavity and thinning of the cortex. Gurlt, on the other hand, considered the bones normal but delicately formed. Charcot, Bruns, and Broca and Herbinet consider it a trophic disease, the lesion being situated in the anterior roots of the spinal cord, and this theory has had considerable weight on account of the similar condition known to occur in certain nervous and mental diseases—in fact, it is the generally accepted explanation. Other observers have considered it caused by disturbed innervation of the arteries of the bone. Schuchardt, and more recently Nathan, have advanced the theory that the disease in young subjects is identical with osteogenesis imperfecta. Many authors consider the disease osteogenesis imperfecta incompatible with extra-uterine life, but although it is a fact that most of the cases are born either prematurely or dead, certain others which are not of an extreme type undoubtedly live (Case II). Nathan reports two cases, in which abnormal fragility was present at birth, both cases living. Zeigler[12] believed the disease of pure congenital origin, due to some malformation of the primary bone cartilage.

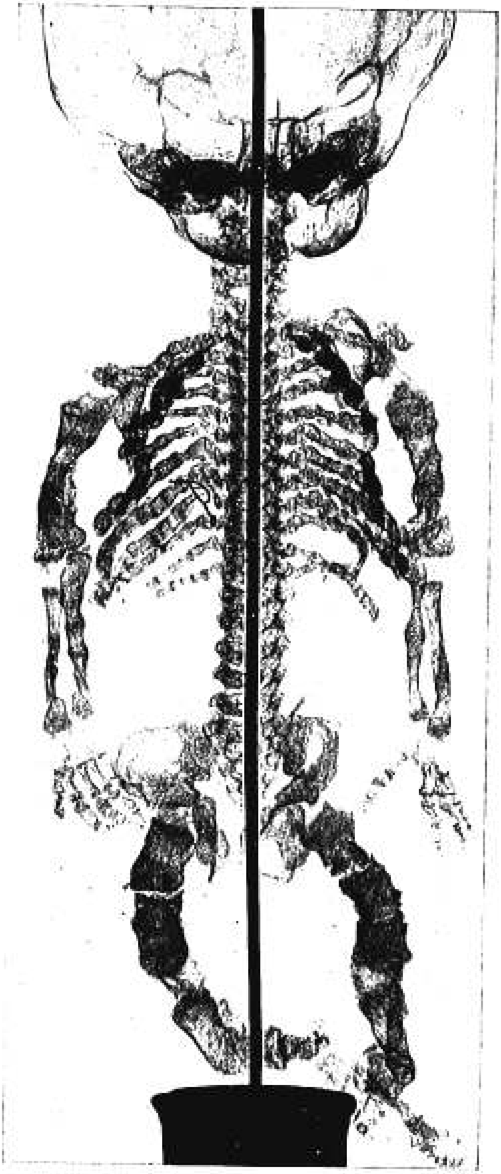
These two cases undoubtedly represent cases of osteogenesis imperfecta which have lived and have no relation to trophic disturbances. The general appearance of Case I at birth was not remarkable, but although the delivery was easy the right humerus was fractured. The fact that no other fracture occurred until the age of five does not entirely eliminate osteogenesis imperfecta, as it is conceivable that the condition may have been present in a mild degree; in fact the number of fractures is not nearly as great as in many of the reported cases. The chief points at present in this case which suggest a congenital origin for the disease are the shape and size of the head, which is similar to that of rickets, and the fact that the posterior fontanelle is open, and it does not seem possible that trophic disturbances having their seat in the anterior horns of the spinal cord could affect the bones of the skull, or prevent the fontanelle from closing. It is unfortunate, as Nathan has pointed out, that the condition of the fontanelles in the reported cases is rarely mentioned. There was not the slightest evidence of syphilis or rachitis in this case.

Case II is similar to Case I in many respects, but the disease is, of course, much more marked. If the two diseases are phases of the same condition, the cause is the same—that is, the theory of disturbance of the primary bone cartilage combined with inability of the epiphyseal cartilage, or periosteum, to form normal bone, as has been shown microscopically, is probably the correct one. The histological appearances of the bone in the two types should, however, be compared carefully, but unfortunately this is almost impossible as adults rarely die of the disease, and will account for most of the cases of idiopathic osteopsathyrosis.

Biggs and many other observers recognize two forms of the disease, one occurring in early life, of which the above cases are the type, and the second occurring in adults. This adult form may on further research prove to be identical with that seen in young people, but it is probably an entirely different disease, possibly of trophic origin. Cases where deformity or bending occurs before fractures are not true cases of idiopathic fragilitas ossium. An hereditary tendency in many of the reported cases has been marked, the disease being transmitted through either parent, and in this respect it is similar to multiple cartilaginous exostoses—a disease of the epiphyseal cartilage, or in some cases of the primary bone cartilage (Lippert[13]). Greenish's[14] case is a marked example of the hereditary tendency.

- Father.
  - Son, 2 fractures..
    - Son, 2 fractures.
    - Son, 2 fractures.
    - 3 normal children.
  - 3 normal children
  - Normal son......
    - Son, 8 fractures.
    - Son, 3 fractures.
    - Son, 4 fractures.
    - Son, 4 fractures.
    - Son, 4 fractures.
    - Daughter, 3 fractures.
    - 4 normal children.

FIG. 6.



Osteogenesis Imperfecta. Radiograph of a skeleton of a still-born infant, showing an incredibly large number of fractures. (Warren Museum).

All the bones of the body, including the cranium, may be involved to a greater or less extent, but the femur, probably on account of its position, is most commonly fractured, next in order coming the bones of the leg and arm.

Symptoms.—The symptoms consist of repeated fractures occurring as the result of insignificant violence or muscular exertion, but are, not rarely, spontaneous. They may occur with great frequency, Blanchard[15] having reported a case with 106 (Fig. 6). The bones may break while the patient is simply standing erect, and it is not uncommon for the patient to awake in the night with pain in the leg to find a fracture, as in Case I. Other than the tendency of the bones to fracture, the subjects are usually in perfect health if they survive the first few years of life.

The symptoms are the same as those of fractures occurring in normal individuals, but differ somewhat in degree. Pain is usually less, and may be insignificant, as illustrated in Case I, by the patient considering the fracture of the olecranon as a slight sprain. Crepitus is said by many to be "soft," but in this case at least did not differ from that of any fracture. Union is usually rapid with but little callous formation, but may be delayed. The deformity is not due to bending of the bones as in osteomalacia or rickets, but, in all true cases, to a faulty reduction of the fracture, and is most marked in the severe cases, the patient becoming resigned to the fact that his bones fracture easily and not seeking treatment, but using the limb before the bony union is solid.

Pathology.—Few of the cases if they survive the first few years of life die of the condition itself; so complete autopsy reports are uncommon. Nothing distinctive has ever been found in the bones, however, the condition being a simple osteoporosis resembling that seen in other diseases and that of osteogenesis imperfecta. The marrow cavity is larger than usual, and the cortex correspondingly thin. Microscopically the trabeculæ are thin, and there may be an increased number of osteoclasts, while the osteoblasts are diminished. The marrow may be normal or may contain an increased amount of fat. The canals are also said to be dilated. Thus there is a true osteoporosis with a reduction in the amount of bone by dilatation of the marrow spaces and canals similar to the form seen in old age or occurring after disease. Chemical examination of the bone shows it to contain a normal proportion of lime and other salts in contradistinction to the bone in osteomalacia, in which there is a diminution of the salts, the bone being replaced by fibrous and osteoid tissue.

Diagnosis.—The diagnosis is made on the symptoms of repeated fractures occurring either spontaneously or after slight violence, other causes of multiple fractures, such as tabes or multiple bone tumors, having been eliminated by the examination and the X-ray.

Prognosis.—The prognosis is on the whole rather unfavorable. The mortality in the first few months of life is extremely high, but in the milder cases there has been a distinct tendency as the child reaches puberty for the bones to become more normal, and the liability to fracture ceases, although in other cases the fractures have occurred with increasing frequency. In those cases where the condition has occurred in adults, there may be a spontaneous cure, or the disease may progress from bad to worse. Ultimate deformity is almost sure to occur.

Treatment.—The treatment directed towards the cure of the disease is unsatisfactory, no drug having any effect. Calcium and phosphorus salts have been largely given in the hope that they would be deposited in the bones, thus strengthening them; but although cases treated in this way have recovered, there is no proof that the cure had any relation to the drugs given. Thyroid extract has been recommended, and largely used, but apparently with little benefit. The patient should be given general tonic treatment in the way of good food, cod liver oil, iron, etc., and kept in the best hygienic surroundings.

What is more important than the general treatment in the present state of our knowledge, is the prophylactic treatment. The patient should be warned of the liability to fracture and protected in every way from violence. Leather or steel braces may be worn, adapted to the individual case, to protect the legs and thighs. When fractures do occur they should be treated as usual, and the greatest care observed as to the position to obviate any unnecessary deformity.

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For further references the reader is referred to Schuchardt, Deutsche Chirurgie, lxxviii, and others of the above mentioned articles.